REMARKS/ARGUMENTS

With entry of this amendment, claims 1, 6, 7, 10-12 and 29, 30, and 37-40 are pending in the above-identified application. Claims 8, 9, and 31-36 are canceled without prejudice, claim 1 is amended, and claim 40 is added as set forth in detail below. No new matter has been added. Applicants reserve the right to pursue claims of original scope in a related, co-pending application. In view of the remarks and amendments set forth herein, examination and reconsideration of all pending claims are respectfully requested.

Examiner Interview & Status of Election/Restrictions

Applicants thank Examiner Ashen and Examiner Wang for the telephonic interview of October 4, 2005, with Kevin Bastian and the undersigned. During the interview, the withdrawal of claims 31-36 as allegedly drawn to a non-elected invention was discussed. While no agreement was reached as to the propriety of this restriction, it was agreed that Applicants would be permitted to pursue embodiments corresponding to claims 31-36 with filing of a Request for Continued Examination under 37 CFR § 1.114.

During a subsequent interview with Examiner Ashen and the undersigned on November 30, 2005, amendments to the claims in accordance with this agreement were discussed. The present amendments serve to enter these amendments. Briefly, claim 1 is amended to recite that the inhibitor is an "analog of a ST3Gal-IV substrate." Support for this amendment is found in the specification is found at, for example, page 13, lines 11-25. Support is also found at page 15, lines 24-26 (stating that competitive inhibitors typically "resemble the substrate or the product(s) and bind the active site of the enzyme, thus blocking the substrate from binding the active site"). In addition, withdrawn claims 31-36 have been canceled.

Double Patenting Rejections

U.S. 6,376,475 in view of Tsuji

Claims 1 and 8-12 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 2, 5, and 8-10 of U.S. Patent No. 6,376,475 in view of Tsuji (*J. Biochem.* 1:1-14, 1996). In maintaining the present rejection, the Examiner has declined to give any weight to the limitation "wherein said animal ... is at risk of developing atherosclerosis or a blood clotting disorder."[1] The Examiner asserts that "all animals are at some level of risk of developing atherosclerosis or a blood clotting disorder."[2] This rejection is overcome in part and traversed in part as set forth below.

Applicants disagree with the Examiner's interpretation of the limitation "at risk of developing atherosclerosis or a blood clotting disorder." According to the Federal Circuit and the MPEP, interpretation of claims during prosecution must be consistent with the interpretation that would be reached by the skilled artisan.[3] Here, particularly in view of the fact that the Examiner's interpretation effectively reads out an express limitation of the claim, it is submitted that the skilled artisan would reasonably understand the limitation at issue to refer to an animal that is at a higher than normal risk of developing atherosclerosis or a blood clotting disorder. Accordingly, Applicants believe the Examiner's interpretation to be inconsistent with the interpretation that the skilled artisan would reach.

While Applicants disagree with the rejection, but in order to expedite prosecution of the instant application, Applicants have amended independent claim 1 to delete reference to an animal "at risk of" developing atherosclerosis or a blood clotting disorder. In view of this amendment to claim 1, dependent claims 8 and 9, directed to prophylactic administration of the inhibitor, have been canceled.

In view of this amendment, Applicants believe the rejection to be obviated. The Examiner has not shown a teaching or suggestion in the art of administering a ST3Gal-IV sialyltransferase inhibitor to an animal "suffering from atherosclerosis or a blood clotting

[1] Office Action dated September 7, 2005, at ¶6, pp. 5 and 6.
[2] *Id.* at p. 6.

disorder," as presently required by the amended claims. Accordingly, even assuming, for arguments sake only, a general motivation to combine Tsuji and claims 1, 2, 5, and 8-10 of U.S. Patent No. 6,376,475, such a combination would not lead the skilled artisan to the invention as presently claimed. Accordingly, withdrawal of the present rejection is respectfully requested.

Co-pending Application No. 10/398,520

Claims 1 and 8-12 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 9-11, and 16-21 of copending Application No. 10/398,520 (also referred to hereinafter as the "'520 application"). The Examiner states that the '520 application and the instant application "are both drawn to a method of administering an ST3Gal-IV sialyltransferase inhibitor that reduces the amounts of a cell-surface sialylated oligosaccharide wherein the sialylated oligosaccharide comprises a terminal α2-3-linked sialic acid."[4] The Examiner further contends that claims in both applications that require co-administration "with a drug for which blood clotting or inflammation is a potential side effect are obvious over each other because both conditions are a result of reducing the level of biosynthesis of alpha 2,3 sialic acid terminated oligosaccharides."[5] This provisional rejection is overcome in part and traversed in part as set forth below.

As noted above with reference to the double patenting rejection in view of U.S. 6,376,475, the claims, as currently amended, recite administration of the ST3Gal-IV sialyltransferase inhibitor to an animal "suffering from atherosclerosis or a blood clotting disorder." Claims 1, 9-11, and 16-21 of the '520 application neither teach nor suggest this limitation. For at least this reason, the present claims are patentable over claims 1, 9-11, and 16-21 of the '520 application.

While the present claims are patentable over claims 1, 9-11, and 16-21 of the '520 application for at least the reason above, Applicants also disagree with the Examiner with regard to dependent claims that require co-administration with a drug for which blood-clotting or

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[3] *See In re Cortright*, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999). *See also* MPEP § 2111.
[4] Office Action dated September 7, 2005, at p. 5.

inflammation is a potential side effect. Irrespective of whether reducing the level of biosynthesis of α2,3 sialic acid terminated oligosaccharides can reduce both inflammation and blood clotting, the recitation of co-administration with a drug for which inflammation is a side effect does not teach or suggest co-administration with a drug for which blood clotting is a side effect because one class of drugs as recited above does not teach or suggest the other.

Nor is there any motivation provided by claims 1, 9-11, and 16-21 of the '520 application to administer the ST3Gal-IV sialyltransferase inhibitor in conjunction with a drug for which blood clotting is a potential side effect. Irrespective of the existence of a common mechanism for reducing inflammation and blood clotting, the '520 claims do not teach or suggest that such a mechanism is shared between inflammation and blood clotting. Thus, the teaching, in the '520 claims, that an inhibitor of ST3Gal-IV sialyltransferase reduces inflammation would not motivate the skilled artisan to co-administer such an inhibitor with a drug for which blood clotting is a potential side effect.

In view of the above, the present claims are patentable over the pending claims of copending Application No. 10/398,520. Withdrawal of the provisional rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

Written Description

Claims 1, 6-12, 29, 30, and 37-39 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. With respect to claims 8 and 9, this rejection is obviated in view of the cancellation of these claims as previously noted. Regarding the remaining claims, this rejection is overcome in part and traversed in part as set forth below.

The Examiner's alleged bases for maintaining the present rejection are generally directed to the following:

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[5] *Id.*

(1) description of an inhibitor of ST3Gal-IV sialyltransferase that will function *in vivo*, so as to provide a method of treatment; and

(2) description of "an animal that is at risk of developing atherosclerosis or a blood clotting disorder," so as to show possession of a method of treating an animal that is at risk of developing atherosclerosis or a blood clotting disorder.[6]

With respect to reason (2), while Applicants disagree with the Examiner, this aspect of the rejection is obviated by the amendment to independent claim 1, as previously noted in response to the double patenting rejections, deleting reference to an animal "at risk of" atherosclerosis or a blood clotting disorder.

As to reason (1), Applicants initially note that the claims as currently amended recite " wherein said inhibitor is an analog of a ST3Gal-IV substrate." Accordingly, Applicants response to the current rejection will address the Examiner's remarks as they pertain to description and state of the art of sialyltransferase inhibitors that are analogs of the enzyme substrate, including the state of the art with respect to obtaining such inhibitors having *in vivo* function.

Applicants also note that the main thrust of the Examiner's argument is that the claimed method relies on *in vivo* function of a ST3Gal-IV inhibitor, and that it is this *in vivo* function for which corresponding structure has allegedly not been described.[7] Thus, the Examiner's argument is focused not on the biological effect of *in vivo* inhibition of ST3Gal-IV activity, which the Examiner appears to acknowledge,[8] but on the nature of the ST3Gal-IV inhibitor itself.

In this regard, the guidance provided in the specification, in view of the knowledge in the art, is sufficient to lead the skilled artisan to analogs of ST3Gal-IV substrates that provide *in vivo* function against ST3Gal-IV. As explained in the specification,

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[6] *See* Office Action dated September 7, 2005, at ¶8, pp. 6-12.
[7] *See id.* at p. 10.

sialyltransferase inhibitors that are analogs of the enzyme substrate were well-known in the art.[9] Such inhibitors include analogs of, *e.g.*, both the donor substrate and acceptor substrate.[10] In this regard, Applicants note that the biochemistry pertinent to glycosyltransferase activity was well-studied as of the effective filing date and continued to be advanced. Concomitantly, the technology associated with the development of glycosyltransferase inhibitors had also matured so that particular approaches were available that are generally applicable to different glycosyltransferases, including sialyltransferases. For example, with respect to sugar nucleotide substrate analogs, it was well-understood that analogs more resistant to enzymatic cleavage at the monophosphate or disphosphate bridge would provide compounds able to selectively inhibit particular glycosyltransferases.[11]

Moreover, such glycosyltransferase inhibitors resembling the enzyme substrate had been used successfully *in vivo* as antiviral and antibiotic agents. Examples of such compounds include the antiviral agent, 2-deoxy-D-glucose, as well as antibiotics such as tunicamycin and streptovirudin.[12] Tunicamycin, for example, is an analog of UDP-GlcNAc, the donor substrate for N-acetylglucosaminyl-transferases. The replacement of the diphosphate bridge with a carbon chain allows tunicamycin to cross the cell membrane but still readily bind the active site of the enzyme.

In light of the knowledge in the art pertaining to substrate analog inhibitors of glycosyltransferases, as summarized above, including the successful *in vivo* use of this class of compounds, the skilled artisan would readily be led to inhibitors of ST3Gal-IV as recited in the claims and that provide *in vivo* inhibitory activity. The design and synthesis of glycosyltransferase inhibitors based on the structure of enzyme substrate(s), was well-known in the art. Further, structurally related compounds had been shown to have *in vivo* activity for other indications. Given this state of the art and the guidance provided in the specification, the skilled

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[8] *See id.* at pp. 24 & 25.
[9] *See* specification at p. 13, ll. 11-25 (citing references).
[10] *See id.* at p. 13, ll. 11-25.
[11] *See, e.g.*, Camarasa *et al.*, *J. Med. Chem.* 28:40-46, 1985 (attached hereto as Exhibit 1).
[12] *See, e.g., id.* at p. 40. *See also* DeClercq, *Biochem. J.* 205:1-13, 1982 (at p. 12) (attached hereto as Exhibit 2)

artisan would reasonably accept "possession" by Applicants of competitive inhibitors of ST3Gal-IV having *in vivo* activity and, therefore, possession of the method as presently claimed.

In this regard, and to address specific remarks of the Examiner, Applicants again note that, according to the Federal Circuit and its predecessor court, the CCPA, Applicants have some flexibility in how "possession" is shown,[13] and that such flexibility is particularly appropriate where the element at issue auxiliary to the invention.[14] The Examiner has stated that it "is not clear how Applicant can argue that [the inhibitors of ST3Gal-IV] are auxiliary to the invention."[15] To clarify Applicants' argument, "auxiliary" in this sense refers to an element of the claim that is not a point of novelty of the invention.[16] In this case, the recited inhibitor of ST3Gal-IV is not the point of novelty of the present invention. Rather, the point of novelty of the claimed invention is the use of such inhibitors to modulate levels of vWF or FVIII in an animal suffering from atherosclerosis or a blood clotting disorder.

Furthermore, Applicants again note the analogy between the presently claimed invention and the decision in *In re Fuetterer*. The Examiner states the following with respect to *Fuetterer*:

> ... the inorganic salts of Fuetterer are not like the sialyltransferase inhibitors required by the method of claim 1. Although they are defined by their ability to carry out a particular function, the inorganic salts of Fuetterer are a broad class of chemically related compounds which the art recognized as being any inorganic salt that had such properties that was usable in his combination. The instant claims are drawn to methods that require the function of a broad class of inhibitors of ST3Gal-IV sialyltransferase enzyme activity *in vivo*, a function that is not art recognized for the broad class of inhibitors of ST3Gal-IV ....[17]

Applicants disagree with the Examiner to the extent that the Examiner would read *Fuetterer* as requiring structural or chemical relatedness among a composition defined

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[13] *See University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886, 1896 (Fed. Cir. 2004).
[14] *See In re Fuetterer*, 138 USPQ 217, 221 (CCPA 1963).
[15] Office Action dated September 7, 2005, at p. 13.
[16] *See Fuetterer*, 138 USPQ at 221.
[17] Office Action dated September 7, 2005, at pp. 14 and 15.

functionally. Applicants also disagree to the extent that the Examiner would read *Fuetterer* as pertaining only to cases were a functional definition applied to all compounds within a chemically related class. Nowhere is it stated in *Fuetterer* that the recited function corresponded to any particular chemically related class of inorganic salts. To the contrary, the court in *Fuetterer* made clear that the functional definition of the inorganic salt would apply to inorganic salts later discovered to have the recited properties.[18] Further, it is clear from the facts of *Fuetterer* that not all inorganic salts would function in accordance with the invention.[19]

Moreover, in view of the knowledge in the art with respect to the design and synthesis of glycosyltransferase inhibitors that are substrate analogs, including the recognition of substrate analogs as a structurally related class of effective inhibitors and the successful *in vivo* use of this structurally related class of inhibitors, it is submitted that the invention as presently claimed requires a function – *inter alia*, *in vivo* activity – that is indeed recognized in the art for the specified class of inhibitors.

Accordingly, for at least the reasons above, Applicants believe the present claims satisfy the written description requirement under 35 U.S.C. § 112, first paragraph. Withdrawal of the rejection is respectfully requested.

Enablement

Claims 1, 6-12, 29, 30, and 37-39 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. With respect to claims 8 and 9, this rejection is obviated in view of the cancellation of these claims as previously noted. Regarding the remaining claims, this rejection is overcome in part and traversed in part as set forth below.

Before addressing the present rejection in detail, Applicants note that the Examiner does not raise any issue with respect to the identification of inhibitory compounds having *in vitro* activity against cells. As stated in Applicants previous response filed June 10,

[18] *See Fuetterer*, 138 USPQ at 223.

2005, screening assays to identify inhibitory compounds were well-known and routine at the time of the present invention, and the Examiner appears to accept this as the state of the art insofar as determination of *in vitro* activity is concerned.

Also, the Examiner has acknowledged that the present specification establishes an *in vivo* biological effect of ST3Gal-IV sialyltransferase enzyme inhibition.[20] The Examiner also accepts that vWF and FVIII were known risk factors for atherosclerosis and blood clotting disorders.[21] Still further, it is noted that no evidence has been provided showing that the skilled artisan would not reasonably accept reduction of vWF or FVIII as a viable targets for amelioration of atherosclerosis or a blood clotting disorder in view of the association of vWF and FVIII with these disorders.

Accordingly, it appears that the issue raised in the present Action is not whether achieving *in vivo* inhibition of ST3Gal-IV would have the claimed biological effect, but whether a class of ST3Gal-IV inhibitors having *in vivo* activity could be identified without undue experimentation by the skilled artisan for use in the method as claimed. It is submitted, as discussed herein, that any experimentation for identifying inhibitors as presently recited would not be considered undue, particularly in view of the history of *in vivo* use of glycosyltransferase inhibitors that are analogs of the enzyme substrate.

To address the Examiner's specific remarks, in maintaining the instant rejection, the Examiner initially refers to the rejection of the claims as allegedly lacking written description.[22] For the reasons previously set forth in Applicants' response to the outstanding written description rejection, Applicants believe the present claims to be adequately described by the specification. Briefly, in light of, *inter alia*, the present amendments and the state of the art in the design and synthesis of sialyltransferase inhibitors, the skilled artisan would be readily led

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[19] *See Fuetterer*, 138 USPQ at 223.
[20] *See, e.g.*, Office Action dated September 7, 2005, at pp. 24 and 25.
[21] *See id.* at p. 24.
[22] Office Action dated September 7, 2005, at p. 15.

to a class of substrate analog inhibitors of ST3Gal-IV enzyme having *in vivo* activity and, therefore, usable in the method as claimed.[23]

The Examiner goes on to set forth the present rejection in the context of factors enumerated in *In re Wands*[24]. In this regard, the Examiner alleged bases for maintaining the instant rejection are generally directed to the following:

> (1) breadth and nature of the invention as a method for *in vivo* treatment or prophylaxis with "any inhibitor";
>
> (2) the extent of the specification's teachings with regard to ST3Gal-IV inhibitors, including species of inhibitors that would function in the claimed method;
>
> (3) the state of the art with respect to ST3Gal-IV inhibitors, particularly antisense molecules and predictability of their use; and
>
> (4) the amount of "*de novo* experimentation" needed to carry out the method.[25]

Each of these factors are addressed in turn below.

First, with regard to the breadth and nature of the invention, Applicants note that the claims as currently amended are directed to the administration of an inhibitor that is an "analog of a ST3Gal-IV substrate" to an animal "suffering from atherosclerosis or a blood clotting disorder." Accordingly, the aspect of the rejection pertaining to prophylactic methods is obviated. Further, the claims recite a class of inhibitors that are structurally related to a substrate of the sialyltransferase. Such a class of inhibitors, including inhibitors with *in vivo* function, is enabled in view of the state of the art as of the effective filing date, for reasons substantially set forth in response to the written description requirement and as further set forth hereinbelow.

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[23] *See* response to written description rejection, *supra*.
[24] 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).
[25] Office Action dated September 7, 2005, at pp. 15-25.

As to the extent of the teachings provided in the instant application, Applicants note that whether particular species of inhibitors are disclosed in the specification is not determinative of whether there is an enabling disclosure. The Examiner has not cited any authority, statutory or otherwise, to suggest that a particular species must be explicitly set forth in the specification to support a generic invention. To the contrary, as stated in the MPEP, "[h]ow a teaching is set forth, by specific example or broad terminology, is not important."[26] Accordingly, what is well-known in the art need not be disclosed in detail in the specification.[27]

Here, in view of the above, it is submitted that the guidance provided in the specification is indeed sufficient in view of the level of knowledge and skill in the art. In particular, the specification explains that sialyltransferase inhibitors that are analogs of the enzyme substrate were well-known in the art,[28] and that such inhibitors include analogs of, *e.g.*, both the donor substrate and acceptor substrate.[29] The specification further cites to various references describing the design and synthesis of substrate analogs for inhibition of sialyltransferases. In view of this disclosure, the essential inquiry for determining enablement of the present claims is whether the state of the art in the design and synthesis of sialytransferase inhibitors that are analogs of the enzyme substrate was advanced enough that the skilled artisan could identify, without undue experimentation, such inhibitory compounds having *in vivo* activity.

In this regard, the field of glycosyltransferase inhibition, using inhibitors that structurally resemble the substrate and including structural considerations for successful *in vivo* use, was well-advanced as of the effective filing date of the instant application. As previously discussed in Applicants' remarks regarding written description, the biochemistry pertinent to glycosyltransferase activity was well-understood, and the technology associated with the development of glycosyltransferase inhibitors based on this biochemistry was also relatively mature. Particular approaches had been developed that are generally applicable to different glycosyltransferases, including sialyltransferases. For example, with respect to sugar nucleotide

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[26] MPEP § 2164.08 (citing *In re Marzocchi*, 439 F.2d 220, 223-4, 169 USPQ 367, 370 (CCPA 1971).
[27] *See* MPEP § 2164.05(a).
[28] *See* specification at p. 13, ll. 11-25 (citing references).
[29] *See id.* at p. 13, ll. 11-25.

substrate analogs, it was well-understood that analogs more resistant to enzymatic cleavage at the monophosphate or disphosphate bridge would provide compounds able to selectively inhibit particular glycosyltransferases.[30] With particular respect to sialyltransferases, as noted in the specification, various substrate analog inhibitors of sialyltransferases were already well-known in the art.[31]

Moreover, substrate analogs of glycosylatransferases, as a structurally related class of inhibitory compounds, had been used successfully *in vivo* for other indications.[32] For example, in the case of the antibiotic tunicamycin, an analog of the donor substrate for N-acetylglucosaminyl-transferases, replacement of the diphosphate bridge with a carbon chain allows tunicamycin to cross the cell membrane but still readily bind the active site of the enzyme. Other examples glycosyltransferase substrate analogs used *in vivo* include, *e.g.*, the antiviral agent, 2-deoxy-D-glucose, as well as the antibiotic streptovirudin.

In view of the above, including the history of *in vivo* use and state of the art in design and synthesis of glycosyltransferase inhibitors, the skilled artisan would reasonably accept that competitive inhibitors of ST3Gal-IV sialyltransferase having *in vivo* activity were readily identifiable for use in the method as claimed.

Further, with regard to the amount of "*de novo*" experimentation required to carry out the method as claimed, it is submitted that any effort in obtaining competitive ST3Gal-IV inhibitors with *in vivo* activity would not be considered undue by the skilled artisan. According to the Federal Circuit and the MPEP, the quantity of any experimentation is not determinative:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.[33]

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[30] *See, e.g.*, Camarasa *et al.* (Exhibit 1).
[31] *See id.* (citing references).
[32] *See id.* at p. 40; *see also* DeClercq (Exhibit 2) at p. 12
[33] *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988); MPEP § 2164.06.

In this case, the specification provides sufficient guidance with respect to the direction in which experimentation should proceed. In particular, the specification shows, using routine assays for assessing factors involving in clotting pathways, that *in vivo* inhibition of ST3Gal-IV sialyltransferase activity decreases levels of vWF or FVIII in an animal without affecting the levels of other hemotstatic factors.[34] The specification further describes methods for identifying candidate inhibitors and points to substrate analogs as one particularly suitable class of inhibitory compounds.[35] The specification also describes the selection of ST3Gal-IV inhibitors by testing for their ability to reduce vWF or FVIII upon administration to laboratory animals,[36] which is standard in the art of drug design. Thus, the skilled artisan would be able to test readily identifiable candidate inhibitors in standard animal models for *in vivo* efficacy on levels of vWF and/or FVIII, which, as noted above, can be assessed using routine assays well-known in the art. Moreover, Applicants submit that the history of *in vivo* use of glycosyltransferase substrate analogs would reasonably be regarded by the skilled artisan as an indication that such inhibitors of ST3Gal-IV would also have *in vivo* activity. Thus, for at least these reasons, the skilled artisan would not consider as undue the identification of a substrate analog inhibitor of ST3Gal-IV having *in vivo* activity.

Accordingly, in view of the above, Applicants believe the present claims to be enabled by the specification under 35 U.S.C. § 112, first paragraph. The claims recite a class of inhibitory compounds that had a history of *in vivo* use and that, in view of the state of the art, were readily identifiable by the skilled artisan at the time of the invention. Furthermore, in light of the knowledge in the art, the specification provides a reasonable amount of guidance to the skilled artisan for how identification of compounds having *in vivo* activity should proceed. Withdrawal of the rejection is respectfully requested.

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[34] *See* specification at, *e.g.*, p. 35, l. 13 to p. 36, l. 5.
[35] *See id.* at p. 13, ll. 11-25, and p. 14, ll. 5-27.
[36] *See id.* at p. 18, ll. 5-9.

Rejections under 35 U.S.C. § 102

Claims 1 and 8-12 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Kapitonov *et al.* (U.S. 6,280,989). The Examiner contends that an "inhibitor of ST3Gal-IV sialyltransferase enzyme activity," as recited in claim 1, is met by the antisense nucleic acid of Kapitonov. The Examiner also asserts that "all animals are inherently at some risk of developing atherosclerosis or a blood clotting disorder."[37] This rejection is overcome in part and traversed in part as set forth below.

First, Applicants disagree with the Examiner's interpretation of the pending claims in relation to the cited art. According to the Federal Circuit and the MPEP, interpretation of claims during prosecution must be consistent with the specification's disclosure as well as with the interpretation those skilled in the art would reach.[38] In the present case, the specification describes "enzyme inhibition" of ST3Gal-IV as involving "the interaction of a substance with an enzyme so as to decrease the rate of the reaction catalyzed by that enzyme."[39] Moreover, inhibition of ST3Gal-IV gene expression via, *e.g.*, antisense nucleic acids, is clearly described in the specification as an embodiment separate from inhibition of "enzymatic activity of the protein."[40] Also, as previously noted in response to the double patenting rejections, Applicants believe the Examiner's interpretation of the phrase, "risk of developing atherosclerosis or a blood clotting disorder," to be inconsistent with the interpretation that the skilled artisan would reach, particularly in view of the fact that such an interpretation effectively reads out an express limitation of the claim.

While Applicants do not agree with the rejection as noted above, the rejection is obviated in view of the present amendments to claim 1 to recite an inhibitor that is an "analog of a ST3Gal-IV substrate" and "wherein said animal is suffering from ~~or is at risk of developing~~ atherosclerosis or a blood clotting disorder." Kapitonov does not disclose administration of a ST3Gal-IV sialyltransferase inhibitor that is an analog of the enzyme substrate. Nor does Kapitonov disclose administration of a ST3Gal-IV sialyltransferase to an animal suffering from

[37] Office Action dated September 7, 2005, at p. 27.
[38] *See In re Cortright*, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999). *See also* MPEP § 2111.
[39] Specification at p. 13, ll. 8-10.

atherosclerosis or a blood clotting disorder. Accordingly, Kapitonov does not anticipate claim 1 as currently amended, nor claims 6, 7, and 10-12 depending therefrom. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 103

Claims 1 and 8-12 stand rejected as allegedly unpatentable over Marth *et al.* (U.S. 6,376,475) in view of Tsuji *et al.* (*J. Biochem.* 1:1-14, 1996). The Examiner, stating that "all animals are inherently at some level of risk of developing atherosclerosis or a blood clotting disorder," has maintained this rejection for reasons set forth in the Action dated February 2, 2005.

While Applicants do not agree with the rejection or reasons for rejection, Applicants believe the rejection to be obviated by the present amendment to independent claim 1, deleting reference to administration of the ST3Gal-IV inhibitor to an animal "at risk of developing" atherosclerosis or a blood clotting disorder. In particular, the Examiner has not shown a teaching or suggestion in the art of administering a ST3Gal-IV sialyltransferase inhibitor to an animal "suffering from atherosclerosis or a blood clotting disorder," as presently required by the amended claims. Accordingly, even assuming, for arguments sake only, a general motivation to combine Marth *et al.* (U.S. 6,376,475) and Tsuji, such a combination would not lead the skilled artisan to the invention as presently claimed.

In view of the above, claims 1, 6, 7, and 10-12 are patentable over Marth *et al.* in view of Tsuji *et al.* under 35 U.S.C. § 103. Withdrawal of the rejection is respectfully requested.

Other Claim Amendments

New claim 40 has been added to more fully claim novel aspects of the present invention. Claim 40 recites a method for "modulating levels of vWF or FVIII in an animal, the method comprising administering to the animal an effective dose of an inhibitor of ST3Gal-IV

[40] *See* specification at p. 12, l. 30, bridging to p. 13, l. 2. *See also, generally*, specification at pp. 13-18.

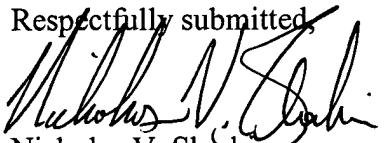
sialyltransferase enzyme activity, wherein said inhibitor is an analog of a ST3Gal-IV substrate and whereby levels of vWF or FVIII in the animal are decreased; and monitoring the animal for levels of vWF or FVIII." Support for this claim is found in the application as filed at, *e.g.*, original claims 1, 2, and 5; page 13, lines 11-25; page 15, lines 24-26; and page 21, lines 21-24. Applicants note that claim 40 is enabled and described by the specification in view of the art for substantially the reasons set forth above with respect to claim 1. Further, Applicants note that none of the cited art teaches or suggests a method comprising the steps as presently recited in claim 40. Accordingly, Applicants believe claim 40 to be allowable.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,



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